Of models and men: recent advances in computational bone tissue engineering

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The creation of man-made living implants is the holy grail of tissue engineering (TE). As basic science advances, one of the major challenges in TE is the translation of the increasing biological knowledge on complex cell and tissue behavior into a predictive and robust engineering process. Mastering this complexity is an essential step towards clinical applications of TE. Computational modeling allows to study the biological complexity in a more integrative and quantitative way. Specifically, computational tools can help in quantifying and optimizing the TE product and process but also in assessing the influence of the in vivo environment on the behavior of the TE product after implantation.

In this talk, I will use the example of bone tissue engineering to demonstrate how computational modeling can contribute in all aspects of the TE product development cycle: cells, carriers, culture conditions and clinics. Depending on the specific question that needs to be answered the optimal model systems can vary from single scale to multiscale. Furthermore, depending on the available information, model systems can be purely data-driven or more hypothesis-driven in nature.

The first example that will be discussed is that of cell culture. Gene regulatory models can help to investigate the stability of specific cell states and their basins of attraction. Furthermore, specific medium compositions can be designed to push cells into a certain state and to keep them there. Both a literature-based and a data-based approach have been developed to capture the processes of chondrogenic differentiation in the growth plate. The second example is that of biomaterial design. In order to optimize bioceramics-based biomaterials for bone tissue engineering, we have developed models simulating the degradation of the biomaterials upon in vivo implantation, as well as the influence the degradation products have on the local biology. Extensive screening experiments have guided the model formation. In turn, the model is used to predict the bone formation capacity of bioceramics-based biomaterials in combination with a specific cell source. For the culture of tissue engineering constructs composed of cells and carriers, bioreactors are used. In order to follow-up the biological events occurring inside the bioreactor, computational models are of great help. We have developed a model capable of simulating neotissue growth in perfusion bioreactors, including the influence of scaffold geometry, fluid flow, oxygen and lactate on the speed of growth. A last example will briefly touch upon the possibilities of computational models in assessing the in vivo effect of specific treatment strategies for bone regeneration. We have developed a model of in vivo bone regeneration with a thorough description of the role of angiogenesis and we are currently testing the effect of a variety of patient properties (defect size, type of trauma, congenital problems) on the regeneration outcome.